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ATTORNEY DOCKET NO. CONFIRMATION NO. APPLICATION NO. FILING DATE FIRST NAMED INVENTOR 11/21/2003 PP-01677.006 1440 10/719,896 John N. Nuss 12/20/2005 EXAMINER 27476 7590 BALASUBRAMANIAN, VENKATARAMAN **Chiron Corporation** Intellectual Property - R440 PAPER NUMBER ART UNIT P.O. Box 8097 Emeryville, CA 94662-8097 1624

DATE MAILED: 12/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

		Application No.	Applicant(s)
		10/719,896	NUSS ET AL.
Office Action Summary		Examiner	Art Unit
		Venkataraman Balasubramanian	1624
The MAILING DATE of this communication appears on the cover sheet with the correspondence address			
Period for Reply			
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION. - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).			
Status			
1) ∑	Responsive to communication(s) filed on 10	May 2005	
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3)			
closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11, 453 O.G. 213.			
Disposition of Claims			
 4)			
5) Claim(s) is/are allowed.			
6)⊠ Claim(s) <u>1-36</u> is/are rejected.			
7) Claim(s) is/are objected to.			
8) Claim(s) are subject to restriction and/or election requirement.			
Application Papers			
9) The specification is objected to by the Examiner.			
10) The drawing(s) filed on is/are: a) accepted or b) objected to by the Examiner.			
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a). Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).			
11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.			
Priority under 35 U.S.C. § 119			
12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) All b) Some * c) None of:			
1. Certified copies of the priority documents have been received.			
2. Certified copies of the priority documents have been received in Application No			
3. Copies of the certified copies of the priority documents have been received in this National Stage			
application from the International Bureau (PCT Rule 17.2(a)). * See the attached detailed Office action for a list of the certified copies not received.			
See the attached detailed Office action for a list of the certified copies not received.			
Attachmen	t(s)		
	e of References Cited (PTO-892)	4) Interview Summary	
	e of Draftsperson's Patent Drawing Review (PTO-948) mation Disclosure Statement(s) (PTO-1449 or PTO/SB/0	Paper No(s)/Mail Da 5) ☐ Notice of Informal Pa	ite atent Application (PTO-152)
Paper No(s)/Mail Date <u>5/20/04, 6/7/04, 7/n/04</u> 6) Other:			

DETAILED ACTION

The preliminary amendment filed on 5/10/2004 is made of record. Claims 1-36 are now pending.

Information Disclosure Statement

References cited in the Information Disclosure Statements (5/20/2004, 6/7/2004, 6/7/2004, 7/12/2004) are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following apply. Any claim not specifically rejected is rejected as it dependent on a rejected claim and shares the same indefiniteness.

1. Recitation of "ester or prodrug thereof" in claim 1 renders claim 1 and its dependent claims 2-36 indefinite. Esters and prodrugs in general and as noted in specification, are compounds, which undergo in vivo hydrolysis to parent active drugs. In that sense recitation of prodrug is acceptable. However, the compound of formula I includes esters and amide groups and therefore it is not clear what is the difference between these groups and the prodrug groups. There is clear-cut ambiguity as to what is to be considered as prodrug and what is not. Applicants should note that if the variable groups are prodrug, which are in general inactive but becomes active upon in

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vivo transformation, then the compound bearing the variable group would be deemed as inactive which is not what the claim recites.

Furthermore, the issue on second paragraph is whether the structures of the claimed compounds are clearly defined. Applicants' "prodrug or ester" are molecules whose structure lie outside the subject matter of formula (I), but upon metabolism in the body are converted to active compounds falling within the structural scope of formula (I). The claim describes the function intended but provides no specific structural guidance to what constitutes a "prodrug". Structural formulas, names, or both can accurately describe organic compounds, which are the subject matter of claim 1. Attempting to define means by function is not proper when the means can be clearly expressed in terms that are more precise.

- 2. Claim 34 is recited twice in the list of claims. See page 136-138 for first recitation and pages 141-143 for second recitation with the same scope. Deletion of second recitation is suggested to avoid double patenting rejection.
- 3. Claims 35 and 36 provide for the use of compound of formula I but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Also note if this claim is intended as a compound claim, then it is a duplicate of claim 1 as there is no structural difference between the two. See Intirtool, LTD. V. Texar Corp., 70 USPQ2D 1780. Note court held that "In general, a claim preamble is limiting if recites essential structure or steps or if it is necessary to give" life.

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meaning, and vitality to claim.'.... However, if the body of the claim describes a structurally complete invention such that deletion of the preamble phrase does not effect the structure or steps of the claimed invention,' the preamble is generally not limiting unless there is clear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art.""

Instant claim 35 if it is a compound claim, is clearly defined by a structure namely a pyrimidine with specific substituents. Omission of the attributes to the compound of genus of claim 35 would not alter the structure of these compounds. Hence, claim 35 will be a duplicate of claim 1.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making prodrug or ester other than those recited as part of variable definition of the claimed compounds. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry - to use the invention. "The factors to be considered in making an enablement rejection have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the

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art and the breadth of the claims", In re Rainer, 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546. a) Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, and produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism 'de novo, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate-and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be biologically active. Thus, determining whether a particular compound meets these three criteria in a clinical trial setting requires a large quantity of experimentation.

There is no working example of a prodrug of a compound the formula (I). The nature of the invention is clinical use of compounds and the pharmacokinetic behavior of substances in the human body. The state of the prodrug art is summarized by Wolff (Medicinal Chemistry). The table on the left side of page 976 outlines the research program to be undertaken to. find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since, the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker (Modem Pharmaceutics) in the first sentence, third paragraph on page

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596 states that "extensive development must be undertaken" to find a prodrug. Wolff (Medicinal Chemistry) in the last paragraph on page 975 describes the artisans making Applicants' prodrugs as a collaborative team of synthetic pharmaceutical chemists and metabolism experts. All would have a Ph. D. degree and several years of industrial experience. It is well established that "the scope of enablement varies inversely degree of unpredictability of the factors involved", 'and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The breadth of the claims includes all of the hundreds of thousands of compounds of formula of claim I as well as the presently unknown list potential prodrug derivatives embraced by the word "prodrug".

Thus, undue experimentation will be required to determine if any particular derivative is, in fact, a prodrug.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Claims 23 2-5 and 26-36 are rejected under U.S.C. 112, first paragraph, because the specification while being enabling for treating breast cancer, does not reasonably provide enablement for treating any or all abnormal cell growth or any or all cancers and

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or any or all proliferation of capillary. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims.

Thé instant method of use claims 26-36 are drawn to "treatment of cancer" and inhibition proliferation of capillaries and the pharmaceutical composition claims 23-25 with intended relate to use for treatment of cancer in general.

As recited, claims 23-36 are reach through claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions for which they lack written description and enabling disclosure in the specification. In the instant case, because of inhibition of phosphotidylinositol (PI)-3- kinase activity in general by compound formula I, it is recited that instant compounds are useful for treatment of any or all disease stated above for which there is no adequate written description and enabling disclosure in the instant specification.

The scope of the claims includes any or all cancer or any or all proliferative capillaries diseases due to phosphotidylinositol (PI)-3- kinase inhibition including those yet to be discovered as due said mode of action for which there is no enabling disclosure. In addition, the scope of these claims includes treatment of various cancers which as recited can include group consisting of lung cancer, bone cancer, pancreatic cancer, skin cancer. cancer of the head or neck, cutaneous or intraocular melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region. stomach cancer, colon cancer, breast cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of

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the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's disease, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, prostate cancer, chronic or acute leukemia, lymphocytic lymphomas, cancer of the bladder, cancer of the kidney or ureter, renal cell carcinoma, carcinoma of the renal pelvis, neoplasms of the central nervous system (CNS), primary CNS lymphoma, spinal axis tumors, brain stem glioma, pituitary adenoma, or a combination of one or more of the foregoing cancers, which is not adequately enabled solely based on the activity of the compounds provided in the specification. The instant compounds are disclosed to have phosphotidylinositol (PI)-3- kinase inhibitory activity and it is recited that the instant compounds are therefore useful in treating any or all diseases stated above for which applicants' provide no competent evidence. It appears that the applicants are asserting that the embraced compounds because of their mode action as phosphotidylinositol (PI)-3- kinase inhibitor that would be useful for all sorts of proliferative capillaries diseases and cancers. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Moreover many if not most of diseases such as psoriasis, lung cancer, brain cancer, pancreatic cancer, colon cancer etc. are very difficult to treat and despite the fact that there are many anticancer drugs.

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The scope of the claims, as generically recited in claim1, includes thousands and thousands of compounds of claim 1 as well as the thousand of diseases embraced by the terms proliferative capillaries and cancer.

Proliferative disease would include benign tumors, malignant tumors, polyps, lumps, lesions, other pre-cancerous conditions, psoriasis, leukemia, the hyper proliferation of the gastric epithelium caused by the Helicobacter pylori infection of ulcers.

Cancer is just an umbrella term. Tumors vary from those so benign that they are never treated to those so virulent that all present therapy is useless.

No compound has ever been found to treat proliferative diseases of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "compound" is contrary to our present understanding of oncology. Cecil Textbook of Medicine states, "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally. Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

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Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Li et al., Breast Cancer Res. Treat. 1-5, 2005, Crowder et al., Breast Cancer Res., 7(5): 212-214, 2005, Nahta et al., Curr. Med. Chem. Anti-Canc. Agents., 3(3) 201-216, 2003(PubMed Abstracts provided).

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

- 1) The nature of the invention: Therapeutic use of the compounds in treating disorders/diseases that require phosphotidylinositol (PI)-3- kinase inhibitory activity.
- 2) The state of the prior art: Recent publications expressed that the phosphotidylinositol (PI)-3- kinase inhibition effects are unpredictable and are still exploratory. See Li et al., Crowder et al., and Nahta et al., cited above which limits the use for breast cancer with reservation.
- 3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical

use for r treating any or all cancers of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

- 4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all cancers or inhibition of any or all proliferative capillaries diseases and the state of the art is that the effects of phosphotidylinositol (PI)-3- kinase activity inhibitors are unpredictable.
- 6) The breadth of the claims: The instant claims embrace any or all proliferative diseases and cancers including those yet to be related to phosphotidylinositol (PI)-3-kinase activity.
- 7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in

the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was 'filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 35 and 36 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and .*Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Cabaj et al., J. Org. Chem. 59, 5090-5092.

Cabaj et al teaches several intermediate compounds, which include compounds embraced in the instant claim. See compound 3, compound 7, compound 8, compound 2a and compound 2c.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Bundy et al.,

J. Med. Chem. 38, 4161-4163

Bundy et al teaches several intermediate compounds, which include compounds embraced in the instant claim. See compound 1and compound 10.

Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Chaudhari et al., WO 02/36586.

Chaudhari et al. teaches several 2,4,6-trisubstituted pyrimidine compounds for treating pain, which include instant compounds. See 4, formula I and note the definition of various variable groups. Especially note when R³ is chosen form E⁶, the compounds taught by Chaudhari et al. include instant compounds. See entire document. See pages 34-46, Table I that shows 125 compounds, which include instant compounds. For example see compound 3, 5, 6,8 etc. which are also generically embraced in the instant claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

- 1. Determining the scope and contents of the prior art.
- 2. Ascertaining the differences between the prior art and the claims at issue.
- 3. Resolving the level of ordinary skill in the pertinent art.
- 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claîm 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chaudhari et al., WO 02/36586.

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Teachings of Chaudhari et al. as discussed in the above 102 rejection is incorporated herein. As noted above, Chaudhari et al. teaches several 2,4,6-trisubstituted pyrimidine compounds for treating pain, which include instant compounds. See 4, formula I and note the definition of various variable groups. Especially note when R³ is chosen form E⁶, the compounds taught by Chaudhari et al. include instant compounds. See entire document. See pages 34-46, Table I that shows 125 compounds, which include instant compounds. For example see compound 3, 5, 6,8 etc. which are also generically embraced in the instant claim.

Chaudhari et al. differs in not exemplifying all compounds generically embraced in compound of formula I.

However, Chaudhari et al. teaches equivalency of those compounds taught in Table 1 with those generically recited in page 4 for compound of formula I.

Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds using the teachings of Chaudhari et al and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer et al., WO 01/72745.

Fischer et al. teaches several pyrimidine compounds for treating psoriasis, which include instant compounds. See page 1, formula 1 and note the definition of various variable groups. Particularly note when R³ is aryl as permitted, the compounds taught

by Fischer et al include instant compounds. See entire document for details of the invention. See pages 6-15 for various species made. See Figure I.

Fischer et al. differs from the instant claims in exemplifying compounds wherein R³ is hydrogen and not exemplifying those compounds where R³ is aryl with or without substituents as required by the instant claim. However, Fischer et al. teaches equivalency of those compounds taught in page 1.

Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds using the teachings of Fischer et al. and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status

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information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

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12/10/2005